Data were collected and analyzed retrospectively using KSGCT database and survey sheets.

Results: Four hundred fifty patients (255 males and 195 females) with a median age of 44-year-old (range 15-68) were included in this study. All patients had underlying hematological malignancies except 13 patients with aplastic anemia. Median serum creatinine level before conditioning was 0.64 (0.32 - 1.33) mg/dl. After correcting the Ccr data by actual body surface area in patients whose body heights and body weights were available, corrected Ccr was 107 (34 - 372) ml/min/1.73m^2. Patients with mildly reduced renal function (< 90 ml/min/1.73 m^2) were further classified into group 1 (23 patients, 5.6%) and group 2 (97 patients, 23.7%), according to the corrected Ccr of 30-59 and 60-89 ml/min/1.73 m^2, respectively. Twenty-four patients (19 patients within 100 days and 5 patients after 100 days) developed severe renal failure which required hemodialysis after HSCT. Hemodialysis was discontinued in 5 patients upon recovery of renal function. Probability of requiring hemodialysis was 13% in the group 1, which was higher than that in the group 2 (2.1%) and that in the normal renal function group (6.6%), but the difference was not statistically significant. The incidences of NRM within 30 days or 100 days after HSCT and grade II to IV acute graft-versus-host disease did not differ among these three groups.

Conclusion: Similarly to the results of HCT-CI analysis, mildly reduced renal function before allogeneic HSCT did not affect the outcome of HSCT.

416

THE STEMEX PHASE II/III STUDY: CHALLENGES IN PRODUCTION AND DELIVERY OF CENTRALLY MANUFACTURED *EX VIVO* EXPANDED UMBILICAL CORD BLOOD (UCB) CD133+ CELLS TO PATIENTS WITH ADVANCED HEMATOLOGICAL MALIGNANCIES

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Use of UCB as an alternative SC source is limited due to inadequate TNC & CD34$^+$ cells, in that it is often difficult to find a single unit for successful engraftment in adolescents & adults. One strategy to overcome this limitation is to increase the number of cells by expansion of HPC. StemEx® was developed as a cell graft based on use of a copper chelator (TEPA) that delays differentiation & promotes expansion of HPC with engraftment capabilities. StemEx is manufactured from a fraction of a single CBU originally frozen in 2 separate fractions. CD133$^+$ progenitor cells purified from the smaller or equal fraction are cultured for 21 days with cytokines & TEPA. The product is transplanted to the patient 24h after infusion of the unmanipulated fraction. A global pivotal Phase II/III registration study is underway to evaluate the safety & efficacy of StemEx in patients with advanced hematological malignancies.

Taking into consideration the variability in the intrinsic potential & the cryopreservation processes of the CBUs, successful & robust manufacturing of clinical batches is one of the major challenges of this study. 61 StemEx batches have been manufactured so far in 3 centralized GMP facilities in US, EU & Israel. All the fresh hand-carried batches were successfully delivered to the centers within the StemEx stability period. Of the 61 batches, 58 successfully passed the in-process & final process quality control (IPQC & FPQC) criteria: median fold expansion of TNC, CD34$^+$ cells & CFU over culture input values were 377 (52-743, n = 58), 74 (6-206, n = 57) & 111 (43-662, n = 56), respectively. Expansion of only a portion of the CBU resulted in a median 9.6 fold increase (0.8-90.3 n = 58) in the total number of CD34$^+$ cells infused, over the theoretical number of CD34$^+$ cells that would be infused from the entire CBU without expansion. Interestingly, all three batches that failed to expand also did not pass the IPQC criteria: ≥ 10 CFU/1000 freshly purified CD133$^+$ cells at day 0 of production. This information, available before initiation of patient myeloablation, provides further confidence regarding the quality of the CBU & the StemEx product.

With the significant production challenges of an *ex vivo* expanded product being successfully met in the current registration trial, StemEx study demonstrates the feasibility of this approach in satisfying an urgent unmet clinical need in the UCB transplantation setting.

417

A NOVEL SEQUENTIAL TREATMENT UTILIZING CPX-351 AS SALVAGE CHEMOTHERAPY FOLLOWED BY A REDUCED INTENSITY CONDITIONING ALLOGENEIC STEM-CELL TRANSPLANTATION FOR PATIENTS WITH REFRACTORY LEUKEMIA

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Cytoreduction followed by Reduced Intensity Conditioning (RIC) may lead to improved results in allogeneic stem cell transplant (SCT) for refractory leukemia. CPX-351 is a novel liposomal formulation that encapsulates the combination of cytarabine and daunorubicin in a fixed 5: 1 ratio. In vitro, it selectively concentrates in the marrow. Clinically, CPX-351 is well tolerated, with a favorable toxicity profile. In a phase I trial, patients with refractory acute leukemia were treated with escalating doses of CPX-351 starting at 60 mg/m2 on days - 28, -26 and -24 followed by RIC with IV busulfan 3.2 mg/kg/day on days -6 to -3 and fludarabine 30 mg /m2/day on days -6 to -3 (Bu/Flu). GVHD prophylaxis with tacrolimus and methotrexate. The protocol was amended to include a second arm, B to shorten the duration prior to stem cell infusion to 3 weeks. Fifteen patients (AML-12, ALL-2, CML in blast crisis-1) have been enrolled to date. Five patients are inevaluable due to short follow up (2), sepsis resulting in aborted transplant plans (2) and donor's unavailability (1). Ten patients underwent SCT are evaluable (AML-8, ALL-2). All patients received HLA compatible grafts (MUD-8, MRD-2). Three patients had primary induction failure and 7 had relapsed refractory disease. All evaluable patients achieved adequate neutrophil engraftment at a mean of 16.6 days (range 12-35). Nine patients achieved adequate platelet engraftment at a mean of 15.8 days (range 11-33). Eight patients achieved complete hematologic and cytogenetic remission upon full blood counts recovery. One patient had full neutrophil and platelets engraftment but did not have a bone marrow biopsy as of this date. Two patients (ALL) had a disease relapse 24 and 60 days post transplant. Acute GVHD occurred in 3 patients. One patient with a stage 2 skin GVHD and 2 patients had stage 3-4 GI GVHD upon cessation of immunosupression 5 and 9 months post transplantation. Grade 3 mucositis developed in 4 patients.The 100 days overall survival and disease free survival for 8 evaluable patients was 85% and 78% respectively. At a mean follow

Table 1. Patient, Disease, and Transplantation Characteristics

Characteristic	Evaluable-10
Age	
Mean	57.5
Range	42-71
Male sex	2
Disease	
AML	8
ALL	2
Time between diagnosis and SCT	
Mean	446.4
Range	161-1683
Donor	
MRD	4
MUD	6
Cohort 1A	6
Cohort 2A	3
Cohort 1B	1
Cycles of chemotherapy prior to SCT	
Mean	4
Range	2-9
Bone marrow blasts at starting CPX	
Mean	50
Range	8-83
Circulating blasts at starting CPX	
Mean	33.4
Range	0-49
CD 34 cell dose infused × 10^6/kg	
Mean	5.9
Range	3.59-10.17